

Concerning obviousness-type double patenting

The rejection of claims 73, 74, 78-80, 84-87 and 89-91 for obviousness-type double patenting over claims 1, 4, and 7 of U.S. Patent No. 5,118,802 has been maintained. In response, Applicants have canceled the aforementioned claims, without prejudice or disclaimer. Accordingly, this rejection may be properly withdrawn. In addition, Applicants have amended claims 75, 81 and 88, which were dependent upon the cancelled claims, simply to convert them to independent format. Claim 92 was also converted to an independent claim and was additionally amended to distinguish the primer oligonucleotide from the extended oligonucleotide (as previously recited in cancelled claim 89), so as to more particularly claim the invention. No new matter has been added by these amendments.

Concerning 35 U.S.C. § 112, second paragraph

Claims 109-111 stand newly-rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for failing to point out any steps in the method of use recited by these claims. In response, and to more particularly point out the claimed subject matter, Applicants hereby amend claim 109 to recite a chain termination method. Support for this amendment can be found on page 3 of the specification at lines 10-11 (first sentence of second full paragraph). The practice of the so-called "Sanger" chain termination method was well-known to those of skill in the art at the time the priority application was filed in January 1984. Moreover, the paragraph bridging pages 3 and 4 of the specification provides a description of the chain termination method for sequencing DNA. Applicants thus maintain that the practice of the chain termination method was and is well-known to those of skill in the art and that claim 109, as amended, particularly points out and distinctly claims the particular aspect of the invention wherein the compositions and methods of the invention are used in a chain termination reaction. Accordingly, Applicants respectfully request withdrawal of this rejection.

Concerning 35 U.S.C. § 102(e) and 35 U.S.C. § 103(a)

Claims 73-107, 109-111 and 118-132 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as allegedly obvious over Ruth, U.S. Patent No. 4,948,882. The Examiner has alleged that the oligonucleotide of Ruth, labeled with fluorescein, meets the structural limitations of the present claims. Citing *In re Fitzgerald et al.*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980) and MPEP 2112-2112.02, the Examiner requires that Applicants show why the oligonucleotide disclosed by Ruth does not inherently possesses the functional limitations of the claimed oligonucleotides.

Assuming, for the purpose of argument, that the fluorescein-labeled oligonucleotide of Ruth meets all of the structural limitations of the present claims (but see below), Applicants submit that the labeled oligonucleotide of Ruth does not necessarily possess all of the functional properties of the presently-claimed tagged oligonucleotides. Applicants wish to point out that the oligonucleotides of the present invention are extendible by a polymerase, as recited, for example, in newly-amended independent claims 75, 81, 88, 92, and in independent claim 98. The ability to be extended by a polymerase is not necessarily an inherent property of the fluorescent-labeled oligonucleotides of Ruth. For example, if the fluorescent-labeled oligonucleotide of Ruth were labeled at or near the 3'-end of the oligonucleotide, it is not clear that such an oligonucleotide could be extended by a polymerase. Interference with polymerase extension could result, in such a case, from effects of the label on base-pairing near the 3'-end of the oligonucleotide, or from effects of the label on the polymerase. For instance, the label might block access of the polymerase to the 3'-end of the oligonucleotide.

Above and beyond the fact that it inherently lacks the functional properties of the claimed oligonucleotides, the fluorescein-labeled oligonucleotide of Ruth does not even meet the structural limitations of the pending claims. There are many ways to produce labeled oligonucleotides, and to say that both Ruth and the inventors provide labeled oligonucleotides

says nothing about the structures of the respective oligonucleotides; even more importantly, such a statement cannot be considered on its face as evidence that the labeled oligonucleotide of Ruth and the claimed labeled oligonucleotides have the same structure. For example, in one embodiment of the present invention, an oligonucleotides is labeled at its 5'-end *via* a nitrogen atom (derived from an amino group). However, none of Ruth's oligonucleotides are labeled at the 5'-end. The oligonucleotide of Ruth is labeled *via* a linker arm that is attached to a base moiety (Ruth at Column 3, lines 56-63, for example). See also Column 6 of Ruth (Formula I), wherein Ruth's preferred oligonucleotides are shown to have a free 5'-end. Nowhere in his specification does Ruth disclose labeling anywhere other than on a base moiety.

Furthermore, the present specification discloses that the tagged oligonucleotides of the invention are capable of being resolved from one another with single-nucleotide resolution. See, for example, page 15, lines 2-4 of the present specification. However, Ruth is silent on the degree of resolution obtained with his fluorescein-labeled oligonucleotide.

Thus not only is the functional limitation "extendible by a polymerase" not an inherent characteristic of the fluorescein-labeled oligonucleotide of Ruth, but the oligonucleotide of Ruth differs structurally from the claimed oligonucleotides. Accordingly, applicants request that the 35 U.S.C. §§ 102(e)/103(a) rejection of claims 73-107, 109-111 and 118-132 be withdrawn.

SUMMARY

Applicants offer the preceding amendments and remarks after careful consideration of the outstanding Office Action, in a sincere effort to address the issues raised therein and to place the pending claims in condition for allowance. Should the Examiner determine that additional matters require discussion, or that a telephone conference would expedite the disposition of this application, s/he is invited to contact the undersigned at (650) 813-5741.

In the unlikely event that the transmittal letter is separated from this document and/or the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 24313-20001.05. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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